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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/061,019	04/15/1998	KATHERINE H. KODAMA	GC272D2	1225

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EXAMINER

RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/19/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant N .

09/061,019

Applicant(s)

KODAMA ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 1998 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Claims 11-18 are currently pending in this application.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Sequence Compliance

Applicant is required to comply with the sequence rules by providing a computer readable sequence disk. See particularly 37 CFR 1.821(d). It appears from the transmittal sheets that applicants intend to transfer the electronic form of the sequence data from the parent application 08/443,954. If so, Examiner requests applicants to provide a separate letter authorizing the Office to transfer the sequence information from the parent to this instant application in order to be fully compliant with sequence rules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 15 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 11, 15 and 18 recites the phrase "secreted polypeptide or a portion thereof". It is not clear to the Examiner as to whether it is essential for

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the “portion” to be functional (i.e., what ever function it inherently possesses) or not. The metes and bounds of the phrase is not clear to the Examiner. For example, if the secreted polypeptide happens to be a glucoamylase, it is not clear to the Examiner whether the portion must have the functional activity of a glucoamylase or not.

Claim 11 and claims 12-18 which depend from claim 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the phrase “a fusion polypeptide comprising from the 5’ end...”. It is not clear to the Examiner as to what applicants mean by “5’ end” with respect to a polypeptide. It is not conventional in the art to refer to the polypeptides in terms of 5’ end or 3’ end. If applicants mean to claim a polypeptide comprising sequences from the “N terminal region/side”, amending the claim accordingly would overcome this rejection.

Claim 11 and claims 12-18 which depend from claim 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the phrase “amino acid sequence encoding a..” in several instances. It is well known in the art that amino acids sequences do not encode a peptide or a polypeptide. Amending the claim by deleting the incorrect phrase and replacing it with the word “comprises” or “comprising” would overcome this rejection.

Claim 11 and claims 12-18 which depend from claim 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 recites the phrase "normally secreted from *Aspergillus*". It is not clear to the Examiner as to what applicants mean by the word "normally". The above phrase renders the claim unclear because it is not clear to the Examiner whether the polypeptide must be secreted by the *Aspergillus* or whether the polypeptide need not be a secreted polypeptide in *Aspergillus*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lawlis (a) et al. (US 5,679,543, issued 10-21-1997, filed 10-5-1994) or Lawlis (b) et al. (US 6,130,063, issued 10-10-2000, filed 10-5-1994) and Kitagawa et al. (BBRC, 1993, Vol. 194(1):375-382.). Claims 11-18 are drawn to a fusion polypeptide wherein the polypeptide comprises from the N-terminal side a signal peptide functional in *Aspergillus*, a secreted polypeptide or a portion thereof secreted from *Aspergillus* sp., an optional cleavable linker sequence followed by a glycosyltransferase having a deletion of the transmembrane anchor domain, wherein the glycosyltransferase is selected from sialyltransferase, galactosyltransferase or fucosyltransferase and wherein the signal peptide sequence is selected from the signal peptides of glucoamylase, α -

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amylase etc., wherein the secreted polypeptide comprises either full length or portion of glucoamylase from *Aspergillus niger* var. *awamori*.

Lawlis(a) et al. or Lawlis (b) et al. teach a fusion protein comprising a signal peptide and a secreted polypeptide or portion thereof from *Aspergillus* further comprising a cleavable linker region and any desired polypeptide sequence which when expressed in a fungal host cell such as *Aspergillus* is expressed at an increased level when compared to a fungal cell expressing such a heterologous polypeptide that is not fused to a secreted *Aspergillus* polypeptide. The reference teaches that the increase in expression is significant such that it can be used for large scale production of heterologous proteins. However, the reference does not teach a fusion polypeptide comprising a glycosyltransferase in which the membrane anchor domain has been deleted as a heterologous polypeptide.

Kitagawa et al. teach the cloning and expression of a human sialyltransferase lacking the first 60 amino acids as fusion protein comprising the human insulin signal sequence in the place of the signal peptide in the instant invention and comprising protein A in place of the secreted *Aspergillus* polypeptide in the instant invention. The reference teaches that such expression provides the sialyltransferase as a soluble protein which can be used for *in vitro* sialylation experiments.

With the above two references in hand, it would have been obvious to one of ordinary skill in the art to make a fusion protein as taught by Lawlis et al. using the sialyltransferase polypeptide taught by Kitagawa et al. in place of the fourth polypeptide sequence in the Lawlis et al. invention. It would also be within the knowledge of those skilled in the art to delete the membrane anchor domain from the sialyltransferase because retaining such a sequence would

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clearly hamper the secretion of the heterologous polypeptide because of the anchoring domain.

One of ordinary skill in the art would have been motivated to do so as sialyltransferases have been known in the art to play an important role glycosylation of recombinant polypeptides and are being used for *in vitro* glycosylation purposes with more demand for pure enzyme and Lawlis et al. teach that expressing heterologous polypeptides as fusion polypeptides according to their teachings increases the yield of the heterologous polypeptide. One of ordinary skill in the art would have a reasonable expectation of success because Lawlis et al. provide methods for making such a polypeptide in general and Kitagawa et al. provide a similar method but less robust than the method of Lawlis et al.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

Claims 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over, Ward et al. (Biotechnology, 1990, Vol 8:435-440) and Kitagawa et al. (BBRC, 1993, Vol. 194(1):375-382.). Claims 11-18 are drawn to a fusion polypeptide wherein the polypeptide comprises from the N-terminal side a signal peptide functional in *Aspergillus*, a secreted polypeptide or a portion thereof secreted from *Aspergillus* sp., an optional cleavable linker sequence followed by a glycosyltransferase having a deletion of the transmembrane anchor domain, wherein the glycosyltransferase is selected from sialyltransferase, galactosyltransferase or fucosyltransferase and wherein the signal peptide sequence is selected from the signal peptides of glucoamylase, α -amylase etc., wherein the secreted polypeptide comprises either full length or portion of glucoamylase from *Aspergillus niger* var. *awamori*.

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Ward et al. teach a fusion polypeptide comprising the signal peptide functional in *Aspergillus* sp. followed by the *Aspergillus* glucoamylase sequence followed by the linker sequence of chymosin which in turn is followed by the bovine chymosin sequence. The reference also teaches that constructing a vector which expresses such a fusion protein and transforming a fungal host cell such as *Aspergillus* results in improved production of the heterologous polypeptide, i.e., the bovine chymosin, when compared to other methods of producing heterologous polypeptides. However, the reference does not teach or suggest fusion polypeptide which comprises signal peptide functional in *Aspergillus* sp. followed by the *Aspergillus* glucoamylase sequence followed by the linker sequence of chymosin which in turn is followed by a glycosyltransferase having a deletion of the transmembrane anchor region.

Kitagawa et al. teach the cloning and expression of a human sialyltransferase lacking the first 60 amino acids as fusion protein comprising the human insulin signal sequence in the place of the signal peptide in the instant invention and comprising protein A in place of the secreted *Aspergillus* polypeptide in the instant invention. The reference teaches that such expression provides the sialyltransferase as a soluble protein which can be used for *in vitro* sialylation experiments.

With the above two references in hand, it would have been obvious to one of ordinary skill in the art to make a fusion protein as taught by Ward et al. using the sialyltransferase polypeptide taught by Kitagawa et al. in place of the chymosin polypeptide. It would also be within the knowledge of those skilled in the art to delete the membrane anchor domain from the sialyltransferase because retaining such a sequence would clearly hamper the secretion of the heterologous polypeptide because of the anchoring domain. One of ordinary skill in the art

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would have been motivated to do so as sialyltransferases have been known in the art to play an important role in glycosylation of recombinant polypeptides and are being used for *in vitro* glycosylation purposes with more demand for pure enzyme and Ward et al. teach that expressing heterologous polypeptides as fusion polypeptides with glucoamylase polypeptide or a portion thereof increases their yield. One of ordinary skill in the art would have a reasonable expectation of success because Ward et al. provide methods for making such a polypeptide in general and Kitagawa et al. provide a similar method but less robust than the method of Ward et al.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-26 of U.S. Patent No. 5,679,543 or claims 17-26 of US 6,130,063 and in view of Kitagawa et al. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined

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application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 11-18 of the instant application are directed to fusion polypeptide comprising from the N-terminal a first, second, third and fourth sequence wherein the first sequence comprises signal peptide functional in *Aspergillus* and the second sequence comprises polypeptide secreted from *Aspergillus* followed by a third and fourth sequence comprising a cleavable linker polypeptide and a glycosyltransferase polypeptide without its membrane anchor domain. Claims 17-26 of both the reference patents while not totally identical to the instant claims are also directed to fusion polypeptide comprising from the N-terminal a first, second, third and fourth DNA sequence wherein the first and second sequences encode *Aspergillus* signal peptide and a polypeptide that can be secreted by *Aspergillus* followed by a third and fourth sequences comprising a cleavable linker polypeptide and the sequence of any desired polypeptide, which encompasses the polypeptide sequence of glycosyltransferase as claimed in the instant claims.

The inventions claimed in the instant application and in the reference patent are similar to one another. The portion of the specification (and the claims) in the reference patents, while broader than the claims in the instant application, includes several embodiments that would anticipate the invention claimed in the instant application. Claims of the instant application listed above cannot be considered patentably distinct over claims 17-26 of the reference patents

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when there is specifically recited embodiment that would anticipate mainly claims 11-18 of the instant application. Alternatively, claims 11-18 cannot be considered patentably distinct over claims 17-26 of the reference patents when there is specifically disclosed embodiment in the instant application that falls within the scope of claims 17-26 of the reference patents because it would have been obvious to one having ordinary skill in the art to combine the teachings of Kitagawa et al. with that of the teachings in the reference patents and slightly modify claims 17-26 of the reference patents by selecting a specifically disclosed embodiment that supports those claims i.e., a fusion protein sequence comprising all the subsequences of those taught in the reference patents except for the last sequence now limited to a glycosyltransferase lacking the transmembrane anchor domain. One of ordinary skill in the art would have been motivated to do this because the Kitagawa et al. reference teaches that recombinant sialyltransferase can be obtained in the soluble form when expressed as a fusion protein.

Conclusion

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.

Manjunath N. Rao, Ph.D.
November 14, 2002


MANJUNATH RAO
PATENT EXAMINER